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Attorney Docket No. PC10244A USA

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By _____
(Signature of person mailing)
Andrea E. Dorigo
(Typed or printed name of person)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF: Obach, R. S.

APPLICATION NO.: 09/528,978

FILING DATE: 3/21/2000

TITLE: USE OF CYP2D6 INHIBITORS IN COMBINATION THERAPIES

Examiner: Jiang

Group Art Unit: 1617

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

SUBMISSION OF DECLARATION UNDER 37 CFR 1.132

Sir:

Applicants submit herewith a Declaration under 37 CFR 1.132 following a telephone communication by Examiner Jiang to the undersigned attorney for Applicants.

A Declaration under 37 CFR 1.132 was originally filed on December 18 2003 together with a Response to the Final Official Action. According to the telephone communication by Examiner Jiang to the undersigned attorney for Applicants referred to above, the Declaration filed was not persuasive. Accordingly, Applicants submit a new Declaration under 37 CFR 1.132, which is enclosed herewith.

In view of the foregoing, allowance of Claim 1, pending in the application, is respectfully requested.

The Commissioner is hereby authorized to charge any fees required under 37 C.F.R. §§1.16 and 1.17 or to credit any overpayment to Deposit Account No. 16-1445.

Respectfully submitted,

Date: April 9, 2004

Andrea Dorigo
Attorney for Applicant(s)
Reg. No. 47,532

Pfizer Inc
Patent Department
150 East 42nd Street – 5th Floor
New York, NY 10017-5755
(212) 733-1898

Patent Application
Attorney Docket No.PC10244A USA

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF:	
R. S. OBACH	:
APPLICATION NO.: 09/528798	:
FILING DATE: March 21 2000	:
TITLE: USE OF A CYP2D6 INHIBITORS IN COMBINATION THERAPIES	:
	:
	:

Mail Stop ____
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. 1.132

Sir:

RONALD SCOTT OBACH, hereby declares, states and says that:

1. He received a B.S. from the State University of New York at Binghamton in 1985, and a Ph.D. from from Brandeis University in 1990.

2. He is currently employed by Pfizer Inc. as a Research Advisor in the Pfizer research facility in Groton, Connecticut, and he has worked at Pfizer Inc. for 11 years.

3. He is familiar with the subject matter of the above-identified application and the references cited therein.

4. The above-identified application is directed to a method of administering the drug (2S,3S)-2-phenyl-3-(2-methoxy-5-trifluoromethoxyphenyl)methylamino-piperidine, or a pharmaceutically acceptable salt thereof, in combination with a CYP2D6 inhibitor, or a pharmaceutically acceptable salt thereof, to a human in need of the intended pharmaceutical activity of the drug, wherein the drug and the CYP2D6 inhibitor are not the same compound.

The CYP2D6 inhibitor may be, for example, quinidine, ajmalacine or pharmaceutically acceptable salts thereof.

5. In the enclosed data for the compound (2S,3S)-2-phenyl-3-(2-methoxy-5-trifluoromethoxyphenyl)methylamino-piperidine, denoted as "CP-B" in the data, Tables 1-4 describe enzymatic kinetic parameters for the metabolism of the compound (including O-demethylation and N-dealkylation) in various mammals, and Table 5 describes the inhibition of the same compound by Cytochrome P450 isoform specific inhibitors. In the figures, Figures 10 and 11 show a correlation between metabolism and inhibition of the same compound using quinidine (Figure 10) and ketoconazole (Figure 11).

6. The foregoing data and figures show a surprising effectiveness of (2S,3S)-2-phenyl-3-(2-methoxy-5-trifluoromethoxyphenyl)methylamino-piperidine in combination with a CYP2D6 inhibitor such as, for example, quinidine or ketoconazole. In particular, the correlation shown in Figures 10 and 11 between the effect on (2S,3S)-2-phenyl-3-(2-methoxy-5-trifluoromethoxyphenyl)methylamino-piperidine of P450 specific inhibitors, such as quinidine and ketoconazole, and the activities of known enzymes such as bufuralol hydroxylase and testosterone hydroxylase would not be obvious due to the unpredictable metabolism of (2S,3S)-2-phenyl-3-(2-methoxy-5-trifluoromethoxyphenyl)methylamino-piperidine. Moreover, taking Figure 10 as an example, the amount of quinidine required to inhibit O-demethylation of (2S,3S)-2-phenyl-3-(2-methoxy-5-trifluoromethoxyphenyl)methylamino-piperidine is suprisingly small – already at about 0.1 µM quinidine there is an approximately 50% drop in the control activity of bufuralol hydroxylase. Similar considerations apply to the inhibition of N-demethylation in Figure 11. Such quantitative effects would be unexpected based on the state of the art.

He further declares that all statements made herein of his own knowledge are true and all statements made on information and belief are believed to be true. All statements made herein are made with the knowledge that willful false statements and the like so made are

punishable by fine or imprisonment or both, under section 1001 of Title 18 of the United States Code, and that willful false statements may jeopardize the validity of the above application or any patent that may issue from it.

Date: 4/15/04

Ronald Scott Obach